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Note on the dynamic instability of microtubules

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Abstract

If the dynamic instability of microtubules follows a gamma distribution then one can associate to it a Cantor set.

Microtubules (MTs), the main protein polymeric filaments of the cell cytoskeleton, are a well-defined biological system where methods in condensed matter, statistical mechanics and the theory of complex systems have been applied. MT dynamics plays an important role in many fundamental cellular processes, such as cell division and cell motility. A peculiar intrinsic dynamics of MTs consisting in extended growth (rescues) and shrinkage (catastrophes) phases of variable duration with rapid switching between these two phases has been known since about a decade [1] and is the subject of many investigations. This spontaneous assembly-disassembly process has been called *dynamic instability* (DI) [1]. It is not clear why MTs should have such a behavior and what is its true origin. There are currently several kinetic models trying to explain DI, both from the side of biologists [2] (based on specific features of the MT hydrolysis involving the GTP and GDP units) and from the side of physicists [3] (based on purely one-step stochastic processes of constant rate).

Recently, Odde, Cassimeris, and Buettner [4] have found a high probability of fitting the published MT length life histories to a gamma distribution ($f(t) = \theta^r t^{r-1} e^{-\theta t}/\Gamma(r)$, where r and θ are the shape parameter and the frequency parameter, respectively, of the distribution) by the Kolmogorov-Smirnov test, for both growth and shrinkage. Their result is not firmly established because the conclusion is based on a small number of phase times (14 growth times and 12 shrinkage times). The exponential distribution still cannot be ruled out. As they remark, other nonnegative probability distributions (Weibull, lognormal, or beta ones) may also be appropriate. However, the property of memory makes all these distributions essentially different from the exponential one. Citing the textbook of Olkin, Gleser, and Derman [5], Odde and collaborators argue that a gamma distribution implies a series of first-order steps from the growth phase to the shrinkage one, with the number of steps given by the shape parameter r of the gamma distribution. For the plus end data, they have found $r = 3$, and thus a series of three first-order transitions each of constant rate θ (≈ 1.7 min^{-1}). This would mean two intermediate metastable states. In their words, "each of these transitions could potentially represent key chemical or physical events occurring in the MT".

The purpose of this note is to point out another connection of the gamma distribution (actually going in the same direction as the aforementioned surmise of Odde *et al*) that makes such a distribution very appealing in the case of MTs, if proven. The connection may be found in the review paper of Carruthers and Shih on the phenomenology of hadronic multiplicity distributions [6]. The point is that the asymptotic form of negative binomial (already written down by Mandel in 1959) is a special case of the gamma distribution (i.e., the case $r = \theta$). Moreover, Carruthers and Shih enumerate possible origins of the negative binomial distribution. The last origin in their list of six items is as a realization of self-similar Cantor set structures. As they commented, the negative binomial distribution can be put into one-to-one correspondence with self-similar

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sequences whose limits lead to the (triadic) Cantor sets. The message of all these connections might well be of great relevance for the MT dynamics, because Cantor sets are directly related to multifractal scaling properties [7] and these would mean self-similar features in the MT dynamic instability. In case the gamma fits of Odde *et al* are confirmed, further studies of the nature of the energetic self-similar trees will be necessary.

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